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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,471	08/31/2006	Philip J. Fay	176/61702	3888

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,471	FAY ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9,11-26,32-46 and 48-52* is/are pending in the application.

4a) Of the above claim(s) *14-18,23-26,32-46 and 48-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9,11-13 and 19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/01/06; 02/05/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election with traverse of Group I, claims 1-6, 9, 11-13, 19-22, in the reply filed on April 7, 2008 is acknowledged. The traversal is on the ground(s) that Lollar does not teach the limitations of the invention, therefore, Lollar cannot destroy unity in this invention. This is not found persuasive because Lollar does teach a modified human factor VIII comprising a point mutation in or at least one calcium binding site of a wild-type factor VIII. On page 12 [0038], the instant specification discloses suitable calcium binding sites that are available for mutation in accordance with the present invention can be located within any one of the A1, A2, A3, C1 and/or C2 domains of the activated wild-type factor VIII. In col. 149, Lollar discloses a modified human factor VIII comprising an amino acid substitution at one or more of position 484, 485, 487, 488, 489, 492, 495, 501, 508, according to SEQ ID NO: 2 (which is human factor VIII). Since the above positions are within the A2 domain, Lollar teaches a modified factor VIII comprising a point mutation in or near at least one calcium binding site of a wild-type factor VIII.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-8, 10, 27-31, 47 are canceled. Claims 14-18, 23-26, 32-46, 48-52 have been withdrawn from further consideration by the Examiner because they are drawn to non-elected inventions. Claims 1-6, 9, 11-13, 19-22 are currently under examination.

Priority: The benefit date is December 3, 2003, for the purpose of prior art.

Claim Objections

Claim 11 is objected to because of the following informalities: claim 11 recites a combination of two or may be more factors. The claim is dependent on claim 1, which appears to recite a single recombinant factor mutant only. Therefore, claim 11 appears to be in improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 6, 9, 11-13, 19-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-2, 6, 9, 11-13, 19-22 are rejected under 112, first paragraph, because it refers to a protein only by function.

The court of Appeals for the Federal Circuit has recently held that such a general definition does not meet the requirements of 35 U.S.C. 112, first paragraph. "A written

description of an invention involving chemical genus, like a description of a chemical species, requires a precise definition, such as be structure, formula {or} chemical name, of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 1997 U.S. App. LEXIS 18221, at *23, quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). The court held that "in claims involving chemical materials, generic formulae usually indicate with specificity what generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish it from others. One skilled in the art therefore cannot, as one can do with a fully described genus visualize the identity of the members of the genus."

Here, Applicants are referring to a product from all sources and species by what it does (i.e. function) rather than what it is (i.e. in terms of structure). There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of factor VIII, beyond human Factor VIII, by any identifying structural characteristics or properties, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants written description of the claimed invention is insufficient to show that the Applicants were in possession of the full scope of the claimed invention.

Further, the "portions thereof," recited in claims 9, 11 is also subject to 112, first paragraph, written description, because the genus of "portions thereof" is even bigger than the genus of Factor VIII point mutants.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 9, 11-13, 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 6 recite a specific activity. It is unclear which specific activity the claims are referring to.

Claims 9, 11 recite portions thereof. It is unclear what is meant by portion and which portion of domains A1, A2, A3, C1, and C2 are being referred to.

Claims 2-5, 12-13, 19-22 are included in this rejection because they are dependent on claim 1 and fail to cure its defect.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-6, 9, 11-13, 19-22 are rejected under 35 U.S.C. 102(a) as being anticipated by Wakabayashi et al. (November 2003 "Residues 110-126 in the Factor VIII Heavy Chain contain a Ca2+ Binding Site required for cofactor activity." Blood (ASH annual meeting abstracts) 102(11): p. 542a, Abstract 1988; IDS 06.01.08). Wakabayashi et al. teach a mutant factor VIII comprising a point mutation at position 113 (E113A) of wild-type factor VIII (p. 542a col. 1; claims 1-6, 9, 12-13, 19, 22).

The elements recited in claims 6, 12, 13 would be inherently present in the mutant factor VIII of Wakabayashi et al. since Wakabayashi et al. teach a mutant factor VIII protein that meets the limitations of instant claim 1.

Claims 1-2, 6, 9, 12-13, 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaufman et al. (US 5422260). Kaufman et al. teach a modified human factor VIII having procoagulant activity comprising at least one to three amino acid substitutions selected from residues 220, 250, 279, 282, 359, etc. (col. 22 lines 23-38; claims 1-2, 6, 9, 12-13). Kaufman et al. also teach pharmaceutical compositions comprising said modified human factor VIII with a pharmaceutically acceptable carrier (col. 24 lines 24-48; claims 19-22). Further, Kaufman et al. teach the modified factor VIII can also comprise a modified inactivation cleavage site, R336K (col. 19 example 5; claim 1).

Claims 1-2, 6, 9, 12-13, 19-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Saenko et al. (US 20050100990). Saenko et al. teach a mutant factor VIII comprising an amino acid substitution at one or more positions selected from Lys(377), His(378), and Lys(466), wherein the mutant factor VIII has procoagulant activity (p. 54 claim 13; claims 1-2, 6, 9, 12-13). Saenko et al. also teach a pharmaceutically acceptable composition comprising the mutant factor VIII combined with stabilizers, delivery vehicles, and/or carriers (p. 13 [0160]; claims 19-22).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Saneko et al. (US 20050100990) in view of Lollar et al. (US 5859204; IDS 06.01.06). The teachings of Saenko et al. are outlined above. Saenko et al. do not teach a hybrid factor VIII.

Lollar et al. disclose functional factor VIII protein comprising a hybrid of factor VIII amino acid sequences from human and a non-human mammal (col. 4 lines 40-65). Lollar et al. disclose hybrid factor VIII can have greater coagulant activity and reduced immunogenic and antigenic activity (col. 3 lines 5-20).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Saenko et al. by substituting the hybrid factor VIII of Lollar

et al. for the factor VIII used in Saenko et al. The motivation to do is given by Lollar et al., which disclose that hybrid factor VIII can have greater coagulant activity and reduced immunogenic activity.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is (571)272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Maryam Monshipouri/

Primary Examiner, Art Unit 1656

December 10, 2008